Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) An isolated polynucleotide which is

a. an isolated polynucleotide comprising a nucleotide sequence encoding a multisubstrate deoxyribonucleoside kinase having at least ~~85%~~ 90% amino acid sequence identity to SEQ ID No. 2 when percentage identity is determined over the entire length of SEQ ID NO:2, or

b. the complement of a.

2. (Currently Amended) The polynucleotide of claim 1, encoding a deoxyribonuleoside kinase enzyme ~~derived from a *Aedes aegypti*~~, which kinase enzyme, ~~when compared to human *Herpes simplex* virus 1 thymidine kinase (HSV-TK1) and~~ upon transformation into ~~an~~ eukaryotic cells, decreases at least four (4) fold more than does human *Herpes simplex* virus 1 thymidine kinase (HSV-TK1) the IC_{50} for inhibition of growth of said cells of at least one nucleoside analogue, as a result of the phosphorylation of said analogue by said kinase.

3 (Cancelled).

4. (Previously Presented) The polynucleotide of claim 1, wherein the isolated polynucleotide comprises the nucleotide sequence of SEQ ID No. 1.

5. (Previously Presented) The polynucleotide of claim 1, wherein the isolated polynucleotide encodes a polypeptide comprising the sequence of SEQ ID No. 2.

6. (Previously Presented) The polynucleotide of claim 1, wherein the isolated polynucleotide is capable of hybridising, under medium stringency conditions, to the complement of a polynucleotide having the nucleotide sequence of SEQ ID No. 1, said isolated polynucleotide encoding a multisubstrate

deoxyribonucleoside kinase.

7. (Previously Presented) The isolated polynucleotide of claim 1, which comprises a polynucleotide sequence having at least 85% nucleotide sequence identity to the polynucleotide sequence presented as SEQ ID NO: 1 when determined over the entire length of SEQ ID NO:1.

8. (Cancelled)

9. (Original) The isolated polynucleotide of claim 1, encoding a C-terminally truncated multisubstrate deoxyribonucleoside kinase.

10. (Withdrawn) An isolated deoxyribonucleoside kinase enzyme encoded by the polynucleotide of claim 1.

11. (Withdrawn) The isolated multisubstrate deoxyribonucleoside kinase of claim 10, being derived from yellow fever mosquito *Aedes aegypti*.

12. (Withdrawn) The isolated deoxyribonucleoside kinase of claim 10, which multisubstrate deoxyribonucleoside kinase enzyme, when expressed and compared to human *Herpes simplex* virus 1 (HSV-TK1) and upon transduction into a eukaryotic cell, decreases at least four (4) fold the IC_{50} of at least one nucleoside analogue.

13. (Withdrawn) The deoxyribonucleoside kinase of claim 10, comprising the amino acid sequence of SEQ ID NO: 2, or an amino acid sequence of at least 85% identity with this sequence, when determined over its entire length.

14. (Withdrawn) The deoxyribonucleoside kinase of claim 10 comprising the amino acid sequence of SEQ ID NO: 2.

15. (Withdrawn) The mosquito deoxyribonucleoside kinase of claim 10, which decreases at least three (3) fold the lethal dose (LD_{100}) of at least one nucleoside analogue when compared to the action of a thymidine kinase derived from human *Herpes simplex* virus 1 (HSV-TK1).

16. (Previously Presented) A vector construct comprising the polynucleotide of claim 1, and a promoter operably linked to the polynucleotide.

17. (Withdrawn) The vector construct of claim 16 which is a viral vector.

18. (Withdrawn) A packaging cell line capable of producing an infective virion comprising the vector of claim 16.

19. (Previously Presented) An isolated host cell genetically modified with the polynucleotide of claim 1.

20. (Previously Presented) The host cell of claim 19, which is a eukaryotic cell.

21. (Withdrawn) The host cell of claim 20, being selected from the group consisting of human stem cell.

22. (Previously Presented) The host cell of claim 19, which is a prokaryotic cell.

23-25. (Cancelled)

26. (Withdrawn) An article comprising a nucleoside analogue and a source of an *Aedes aegypti* derived deoxyribonucleoside kinase for the simultaneous, separate or successive administration in cancer therapy.

27. (Withdrawn) Article according to claim 26, wherein the nucleoside analogue is a cytidine analogue.

28. (Withdrawn) Article according to claim 26, wherein the nucleoside analogue is Gemcitabine or AraC.

29. (Withdrawn) Article comprising a nucleoside analogue and a source of a deoxyribonucleoside kinase for the simultaneous, separate or successive administration in cancer therapy, wherein the source of deoxyribonucleoside kinase comprises the nucleotide sequence of claim 1.

30. (Withdrawn) Article comprising a nucleoside analogue and a source of a deoxyribonucleoside kinase for the simultaneous, separate or successive administration in cancer therapy, wherein the source of deoxyribonucleoside kinase comprises the polypeptide of claim 10.

31. (Withdrawn) Article comprising a nucleoside analogue and a source of a deoxyribonucleoside kinase for the simultaneous, separate or successive administration in cancer therapy, wherein the source of deoxyribonucleoside kinase

comprises the host cell of claim 19.

32. (Withdrawn) Article comprising a nucleoside analogue and a source of a deoxyribonucleoside kinase for the simultaneous, separate or successive administration in cancer therapy, wherein the source of deoxyribonucleoside kinase comprises the packaging cell line of claim 18.

33. (Withdrawn) A method of sensitising a cell to a nucleoside analogue prodrug, which method comprises the steps of

(i) transfecting or transducing said cell with a polynucleotide sequence according to claim 1 encoding a deoxyribonucleoside kinase enzyme, that promotes the conversion of said prodrug into a (cytotoxic) drug; and

(ii) delivering said nucleoside analogue prodrug to said cell;

wherein said cell is more sensitive to said (cytotoxic) drug than to said nucleoside analogue prodrug.

34. (Withdrawn) The method of claim 33, wherein the nucleoside analogue is a cytidine analogue.

35. (Withdrawn) The method of claim 33, wherein the nucleoside analogue is gemcitabine (dFdC) or AraC.

36. (Withdrawn) A method of inhibiting a pathogenic agent in a warm-blooded animal, which method comprises administering to said animal a polynucleotide of claim 1.

37. (Withdrawn) The method of claim 36, wherein said polynucleotide sequence or said vector is administered *in vivo*.

38. (Withdrawn) The method of claim 36, wherein said pathogenic agent is a virus, a bacteria or a parasite.

39. (Withdrawn) The method of claim 36, wherein said pathogenic agent is a tumor cell.

40. (Withdrawn) The method of claim 36, wherein said pathogenic agent is an autoreactive immune cell.

41. (Withdrawn) The method of claim 36, further comprising the step of administering a nucleoside analogue to said warm-blooded animal.

42. (Withdrawn) The method of claim 41, wherein said nucleoside analogue is a cytidine analogue.

43. (Withdrawn) The method of claim 41, wherein said nucleoside analogue is gemcitabine (dFdC), or AraC.

44-45. (Cancelled)

46. (Withdrawn) A method of phosphorylating a nucleoside or a nucleoside analog, comprising the steps of

i) subjecting the nucleoside or nucleoside analog to the action of the deoxyribonucleoside kinase enzyme of claim 10, and

ii) recovering the phosphorylated nucleoside or nucleoside analog.

47. (Withdrawn) The method of claim 46, wherein the nucleoside or nucleoside analog is a purine.

48. (Withdrawn) A method of non-invasive nuclear imaging of transgene expression of a deoxyribonucleoside kinase enzyme in a cell or subject, which method comprises the steps of

(i) transfecting or transducing said cell or subject with a polynucleotide sequence encoding the deoxyribonucleoside kinase enzyme of claim 10, which enzyme promotes the conversion of a substrate into a substrate-monophosphate;

(ii) delivering said substrate to said cell or subject; and

(iii) non-invasively monitoring the change to said prodrug in said cell or subject.

49. (Withdrawn) The method of claim 48, wherein the monitoring carried out in step (iii) is performed by Single Photon Emission Computed Tomography (SPECT), by Positron Emission Tomography (PET), by Magnetic Resonance Spectroscopy (MRS), by Magnetic Resonance Imaging (MRI), or by Computed Axial X-ray Tomography (CAT), or a combination thereof.

50. (Withdrawn) The method of claim 48, wherein the substrate is a labelled nucleoside analogue.

51-54. (Cancelled)

55. (Previously Presented) A method of preparing a deoxyribonucleoside kinase enzyme comprising culturing a host cell genetically modified with a polynucleotide of claim 1, encoding said enzyme in expressible form, and recovering the enzyme from the culture medium and/or the cells.

56. (Cancelled).

57. (Previously Presented) The polynucleotide of claim 1 wherein said polypeptide comprises an amino acid sequence which has at least 95% identity to SEQ ID NO:2.

58. (Previously Presented) The polynucleotide of claim 1 wherein said polypeptide comprises an amino acid sequence which has at least 98% identity to SEQ ID NO:2.

59. (Currently Amended) The polynucleotide of claim 1 wherein the polypeptide comprises an amino acid sequence which differs from SEQ ID NO:2, if at all, solely by amino acid replacement of one or more semi-conserved or non-conserved residues, wherein,

1) the conserved residues are: M1, A2, A4, I5, E8, R9, L10, G11, G14, K15, K16, P17, F18, T19, V20, F21, E23, G24, N25, I26, G27, S28, G29, K30, T31, T32, F33, L34, N35, H36, F37, E38, K39, F40, K41, D42, C45, L46, L47, T48, E49, P50, V51, E52, K53, W54, R55, C57, G58, G59, V60, N61, L62, L63, L65, M66, Y67, K68, P70, H71, W73, A74, M75, P76, F77, Q78, Y80, V81, T82, L83, T84, M85, L86, M88, H89, T90, T93, D94, K95, S96, V97, K98, L99, M100, E101, R102, S103, F105, S106, A107, R108, Y109, C110, F111, V112, E113, N114, M115, L116, G119, S120, L121, H122, Q123, G124, M125, Y126, N127, L129, Q130, E131, W132, Y133, F135, I136, N139, I140, H141, I142, Q143, A144, D145, L146, I147, V148, Y149, L150, R151, T152, S153, P154, E155, V157, Y158, E159, R160, K162, R164, A165, R166, S167, E168, E169, S170, C171, V172, P173, L174, K175, Y176, L177, Q178, E179, L180, H181, E182, L183, H184, E185, W186, L187, I189, H190, G191, P194, R195, A197, P198, V199, L200, V201, L202, D203,

A204, D205, L206, D207, L208, N210, I211, E214, Y215, K216, R217, S218, E219, T220, S221, I222, L223, K224, P225, I226, L227, I228, N230, T231, N232, Q233, H234, P235, I236, L237, S239, P240, S241, K242, R243, R245, and T246,

2) the semi-conserved residues are: I22, V44, D64, E69, R72, T79, M104, I128, I156, M161, S213, S244, and E247, and

3) the non-conserved residues are ~~neither (1) or (2)~~ A3, G6, P7, V12, A13, R43, D56, N87, Y91, Q92, A117, S118, E134, H137, A138, K163, L188, T192, F193, V196, H209, S212, D229, A238, and F248.

60. (Cancelled).

61. (Currently Amended) The polynucleotide of claim 1 wherein the polypeptide comprises an amino acid sequence which differs from SEQ ID NO:2, if at all, solely by amino acid replacement of one or more non-conserved residues,
wherein 1) the conserved residues are: M1, A2, A4, I5, E8, R9, L10, G11, G14, K15, K16, P17, F18, T19, V20, F21, E23, G24, N25, I26, G27, S28, G29, K30, T31, T32, F33, L34, N35, H36, F37, E38, K39, F40, K41, D42, C45, L46, L47, T48, E49, P50, V51, E52, K53, W54, R55, C57, G58, G59, V60, N61, L62, L63, L65, M66, Y67, K68, P70, H71, W73, A74, M75, P76, F77, Q78, Y80, V81, T82, L83, T84, M85, L86, M88, H89, T90, T93, D94, K95, S96, V97, K98, L99, M100, E101, R102, S103, F105, S106, A107, R108, Y109, C110, F111, V112, E113, N114, M115, L116, G119, S120, L121, H122, Q123, G124, M125, Y126, N127, L129, Q130, E131, W132, Y133, F135, I136, N139, I140, H141, I142, Q143, A144, D145, L146, I147, V148, Y149, L150, R151, T152, S153, P154, E155, V157, Y158, E159, R160, K162, R164, A165, R166, S167, E168, E169, S170, C171, V172, P173, L174, K175, Y176, L177, Q178, E179, L180, H181, E182, L183, H184, E185, W186, L187, I189, H190, G191, P194, R195, A197, P198, V199, L200, V201, L202, D203, A204, D205, L206, D207, L208, N210, I211, E214, Y215, K216, R217, S218, E219, T220, S221, I222, L223, K224, P225, I226, L227, I228, N230, T231, N232, Q233, H234, P235, I236, L237, S239, P240,

S241, K242, R243, R245, and T246,

2) the semi-conserved residues are: I22, V44, D64, E69, R72, T79, M104, I128, I156, M161, S213, S244, and E247, and

3) the non-conserved residues are ~~neither (1) or (2)~~ A3, G6, P7, V12, A13, R43, D56, N87, Y91, Q92, A117, S118, E134, H137, A138, K163, L188, T192, F193, V196, H209, S212, D229, A238, and F248.

62. (Cancelled).

63. (Previously Presented) The polynucleotide of claim 1 wherein the polypeptide comprises an amino acid sequence which differs from SEQ ID NO:2, if at all, solely by one or more of the following substitutions:

(i) substitution of an amino acid selected from the group consisting of Ala, Leu, Ile, Val, Pro, Met, Phe and Trp for another of that group,

(ii) the substitution of an amino acid selected from the group consisting of Ser, Thr, Tyr, Asn, Gln and Cys for another of that group,

(iii) the substitution of an amino acid selected from the group consisting of Lys, Arg and His for another of that group, and

(iv) the substitution of Asp for Glu or vice versa.

64. (Currently Amended) The polynucleotide of claim 1 wherein said polypeptide ~~is characterized by~~ comprises an amino acid sequence identical to SEQ ID NO:2.

65. (Currently Amended) An isolated polynucleotide which is

c) an isolated polynucleotide comprising a nucleotide sequence encoding a multisubstrate deoxribonucleoside kinase, and capable of hybridizing to the complement of a polynucleotide having the nucleotide sequence of SEQ ID No. 1,

under medium stringency conditions, or d) a complement thereof.

66. (Previously Presented) The polynucleotide of claim 65 wherein the hybridization occurs under conditions of medium/high stringency.

67. (Previously Presented) The polynucleotide of claim 65 wherein the hybridization occurs under conditions of high stringency.

68. (Previously Presented) The polynucleotide of claim 65 wherein the hybridization occurs under conditions of very high stringency.

69. (Previously Presented) The polynucleotide of claim 7 which comprises a polynucleotide sequence having at least 90% nucleotide sequence identity to SEQ ID NO:1.

70. (Previously Presented) The polynucleotide of claim 7 which comprises a polynucleotide sequence having at least 95% nucleotide sequence identity to SEQ ID NO:1.

71. (Previously Presented) The polynucleotide of claim 7 which comprises a polynucleotide sequence having at least 98% nucleotide sequence identity to SEQ ID NO:1.

72. (Previously Presented) The polynucleotide of claim 7 which is identical to SEQ ID NO:1.

73-75. (Cancelled).

76 (new). The polynucleotide of claim 1, encoding a deoxyribonuleoside kinase enzyme, which kinase enzyme, upon transformation into an eukaryotic cell, decreases at least ten fold more than does human *Herpes simplex* virus 1 thymidine kinase (HSV-TK1) the LD100 of at least one nucleoside analogue against said cell as a result of the phosphorylation of said analogue by said kinase.